(v) Its loss on drying is not more than 1.5 percent.

(vi) Its pH in an aqueous solution containing 60 milligrams per milliliter is not less than 5.0 and not more than 7.5.

(vii) Its penicillin G content is not less than 80.8 percent and not more than 94.3 percent.

(viii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, loss on drying, pH, penicillin G content, and crystallinity.

(ii) Samples required:

(*a*) If the batch is packaged for repacking or for use in the manufacture of another drug:

(*1*) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

(*2*) For sterility testing: 20 packages, each containing approximately 600 milligrams.

(*b*) If the batch is packaged for dispensing:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Sample preparation.* Dissolve an accurately weighed portion of the sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration; also, if it is packaged for dispensing, reconstitute as directed in the labeling. Then using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single-dose container; or if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute with solution 1 to give a stock solution of convenient concentration.

(ii) *Assay procedures.* Use any of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(*a*) *Microbiological agar diffusion assay.* Proceed as directed in §436.105 of this chapter, diluting an aliquot of the stock solution with solution 1 to the reference concentration of 1.0 unit of penicillin G per milliliter (estimated).

(*b*) *Iodometric assay.* Proceed as directed in §436.204 of this chapter, diluting an aliquot of the stock solution with solution 1 to the prescribed concentration.

(*c*) *Hydroxylamine colorimetric assay.* Proceed as directed in §436.205 of this chapter.

(2) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in §436.32(b) of this chapter, using a solution containing 20,000 units of penicillin G per milliliter.

(4) [Reserved]

(5) *Loss on drying.* Proceed as directed in §436.200(b) of this chapter.

(6) *pH.* Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 60 milligrams per milliliter.

(7) *Penicillin G content.* Proceed as directed in §436.316 of this chapter.

(8) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

[42 FR 59860, Nov. 22, 1977, as amended at 45 FR 16472, Mar. 14, 1980; 45 FR 22922, Apr. 4, 1980; 50 FR 19918, 19919, May 13, 1985]

§440.81a Sterile penicillin G sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Penicillin G sodium is sodium 3,3-dimethyl-7-oxo-6-(2 - phenylacetamido) - 4 - thia - 1 - azabicyclo [3.2.0] heptane-2-carboxylate. It is so purified and dried that:

(i) Its potency is not less than 1,500 units and not more than 1,750 units per milligram. If it is packaged for dispensing, its content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of units of penicillin G that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its loss on drying is not more than 1.5 percent.

(vi) Its pH in an aqueous solution containing 60 milligrams per milliliter is not less than 5.0 and not more than 7.5.

(vii) Its penicillin G content is not less than 84.5 percent and not more than 98.5 percent.

(viii) It is crystalline.

(ix) It passes the test for heat stability if it does not show a loss of more than 10 percent of its original potency.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, loss on drying, pH, penicillin G content, crystallinity, and heat stability.

(ii) Samples required:

(*a*) If the batch is packaged for repacking or for use in the manufacture of another drug:

(*1*) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

(*2*) For sterility testing: 20 packages, each containing approximately 600 milligrams.

(*b*) If the batch is packaged for dispensing:

(1) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Sample preparation.* Dissolve an accurately weighed portion of the sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration; also, if it is packaged for dispensing, reconstitute as directed in the labeling. Then using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single-dose container; or if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative aliquot from each container. Dilute with solution 1 to give a stock solution of convenient concentration.

(ii) *Assay procedures.* Use any of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(*a*) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, diluting an aliquot of the stock solution with solution 1 to the reference concentration of 1.0 unit of penicillin G per milliliter (estimated).

(*b*) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, diluting an aliquot of the stock solution with solution 1 to the prescribed concentration.

(*c*) *Hydroxylamine colorimetric assay.* Proceed as directed in § 436.205 of this chapter.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 20,000 units of penicillin G per milliliter.

(4) [Reserved]

(5) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 60 milligrams per milliliter.

(7) *Penicillin G content.* Proceed as directed in § 436.316 of this chapter.

(8) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

(9) *Heat stability.* Proceed as directed in § 436.214 of this chapter.

[42 FR 59861, Nov. 22, 1977, as amended at 45 FR 22922, Apr. 4, 1980; 50 FR 19918, 19919, May 13, 1985]

§ 440.83a Sterile piperacillin sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Sterile piperacillin sodium is the sodium salt of (2*S*,5*R*, 6*R*)-6-[(*R*)-2-(4-ethyl-2,3-dioxo-1-piperazine-carboxamido)-2-phenylacetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo-[3.2.0]heptane-2-carboxylate. It is so purified and dried that:

(i) Its potency is not less than 863 micrograms and not more than 1,007